

Appl. No.:10/813,467  
Atty. Dkt. No.:10031551-1

**REMARKS**

In view of the following remarks, the Examiner is requested to withdraw the rejections and allow Claims 28-59 and 61, the only claims pending and currently under examination in this application.

***Claim Rejections - 35 USC § 102(b)***

Claims 28-36, 38-44, 46-48, 50-52, 54-59, and 61 were rejected under 35 U.S.C. 102(b) as being anticipated by Anderson et al (US Patent No. 5,186,824, Issued 16 February 1993).

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegeal Bros. v. Union Oil of California*, 814 F.2d 628, 631; 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987).

The claims at issue are directed to a method of producing an addressable array. Pg. 10, lines 13-26 of the specification in the present case state that an "array is 'addressable' when it has multiple regions of different moieties (e.g., different polynucleotide sequences) such that a region (i.e., a "feature" or "spot" of the array) at a particular predetermined location (i.e., an "address") on the array will detect a particular target or class of targets (although a feature may incidentally detect non-targets of that feature)."

In maintaining this rejection, the Examiner alleges that Anderson et al teaches a membrane incorporating interactive particles (column 6, lines 49-56), wherein the interactive particles are the different locations on the surface of the membrane, which is the substrate. The Examiner further alleges that the interactive particles are porous beads (column 21, line 66 - column 22, line 3). The Examiner alleges that the porous beads have different moieties, in the form of different individual molecules, attached thereon. The Examiner further alleges that since the porous beads are incorporated on the membrane, the locations of the beads are predetermined. As such, the Examiner alleges that the porous beads on the

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membrane are therefore an addressable array in accordance with the definition of an addressable array on page 10, lines 13-26 of the specification.

As such, the Examiner's continued rejection is based on the conclusion by the Examiner (which is unsupported by a specific citation to a location in the Anderson publication) that: "since the porous beads are incorporated on the membrane, the locations of the beads are predetermined."

Applicants can find no teaching anywhere in the Anderson disclosure that the locations of the beads in the membrane is predetermined. Furthermore, there is no teaching or suggestion in Anderson as to how one would make a membrane with beads incorporated at predetermined locations. Anderson is completely silent as to the location of specific beads and specific locations in the membrane. It is just as likely based on Anderson's silence with respect to this point that the beads are not present at known predetermined locations but incorporated in a spatially random manner into the membrane.

In the absence of any specific teaching of locations of beads at predetermined locations, the Examiner's conclusion regarding the locations of the beads in the membranes being predetermined is not supported.

Accordingly, Anderson's asserted teaching of membrane incorporating porous beads is not equivalent to an addressable array of oligonucleotides on a substrate.

Furthermore, according to the procedure described under the heading, "Oligonucleotide Synthesis," (column 19, line 40 - column 20, line 9), it is not possible to produce an addressable array of oligonucleotides by the method of Anderson et al.

Anderson et al does not discriminate with respect to the spatial positioning of the nucleotide monomers from which the oligonucleotides are grown. Anderson et al teaches that the nucleotides are attached without specifying a method for attaching the nucleotides to predetermined positions. "Activation and attachment of the first

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nucleotide (controlled-pore glass (CPG) is commercially available with the first nucleotide already attached, making this step unnecessary in practice)." (Column 19, lines 55-58). As such, the nucleotide monomers will indiscriminately be attached to the interactive particles cited by the Examiner. Anderson et al is silent with respect to determining the positioning of the first nucleotide monomers before attaching the subsequent nucleotide monomers. As such, Anderson et al does not teach a method for producing oligonucleotides in a particular predetermined location.

Because Anderson et al does not teach a method for producing oligonucleotides in a particular predetermined location, Anderson et al fails to teach the production of an addressable array of oligonucleotides. As such, Anderson et al fails to teach the element of claims 28 and 56 of a method for producing an addressable array of oligonucleotides on a substrate.

It is furthermore not possible to produce an addressable array as claimed by the method of Anderson et al because the function of the rotary processor is to produce a downstream output of phase separated oligonucleotides. Anderson et al teaches that the product polymer is immobilized while the failed sequence is eluted away from the product. Column 20, lines 15-19 of Anderson states that "if purification is required, the product is adsorbed on a small reverse phase column, the failure sequences eluted, after which the dimethoxytrityl (DMT) group, by which the product is absorbed to the column, is removed from the support-bound oligonucleotides." Anderson et al explicitly states that the failure sequence is eluted away from the support-bound oligonucleotide. The failure sequence is therefore not bound to the same support as the support-bound oligonucleotide. As such, the product and the failed sequence are not covalently bonded to a surface of a substrate as an array.

The inclusion of this chromatographic separation step (column 20, lines 15-19) in the procedure outlined under the heading, "Oligonucleotide Synthesis", explicitly teaches the opposite of producing an addressable array of oligonucleotides. According to the invention in Anderson et al, the oligonucleotides generated inside

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the rotary processor are cleaved from the solid phase supports and separated by fluid-phase chromatography.

As such, Anderson fails to teach a method of producing an addressable array as claimed.

Accordingly, the rejection of claims 28-36, 38-44, 46-48, 50-52, 54-59, and 61 as being anticipated by Anderson under 35 U.S.C. § 102 (b) should be withdrawn.

***Claim Rejections - 35 USC § 103(a)***

Claims 28 and 37 are rejected under 35 U.S.C. §103(a) as being unpatentable over Anderson et al (US Patent No. 5,186,824, issued February 16, 1993) in view of Greene et al (*Protective Groups in Organic Synthesis*, 3<sup>rd</sup> ed., Wiley and Sons, New York, 1999, page 106).

As explained above, Anderson et al fails to teach the production of an addressable array of oligonucleotides because Anderson et al does not discriminate with respect to the deposition and spatial positioning of the first nucleotide monomer.

Furthermore, Anderson et al fails to suggest the production of an addressable array of oligonucleotides.

In fact, Anderson et al teaches the opposite of producing an addressable array of oligonucleotides. Anderson teaches of the opposite of producing an addressable array because none of the monomers are attached to any specific predetermined locations, but instead are randomly deposited on the substrate surface. The inclusion of the chromatographic separation step (column 20, lines 15-19) in the procedure outlined under the heading, "Oligonucleotide Synthesis", further teaches the opposite of producing an addressable array of oligonucleotides. According to Anderson et al, the oligonucleotides generated inside the rotary processor are cleaved from the solid phase supports and separated by fluid-phase chromatography.

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As such, Anderson et al fail to teach or suggest the production of an addressable array and in fact teaches away from the production of an addressable array.

As Greene was cited solely for its asserted teaching of purging with a higher density fluid, Greene fails to make up for the above deficiency in Anderson.

Accordingly, claims 28 37 are not obvious under 35 U.S.C. §103 (a) over Anderson in view of Greene and this rejection should be withdrawn.

The Examiner next rejected claims 28 and 44-45 under 35 U.S.C. §103(a) as being unpatentable over Anderson et al in view of Mian et al (US Patent No. 6,319,469 issued November 20, 2001). As reviewed above, Anderson et al fails to teach or suggest the production of an addressable array of oligonucleotides. As Mian was cited solely for a disclosure of flow rates, Mian fails to make up the deficiency in Anderson. Accordingly, claims 28 and 44-45, are not obvious under 35 U.S.C. §103 (a) over Anderson in view of Mian and this rejection should be withdrawn.

The Examiner rejected claims 28-29 and 49 under 35 U.S.C. §103(a) as being unpatentable over Anderson et al in view of Gamble et al (US Patent No. 5,874,554, issued February 23, 1999). As explained above, Anderson et al fails to teach or suggest the production of an addressable array of oligonucleotides. As Gamble was cited solely for this disclosure of pulse-jet deposition, Gamble fails to make up this deficiency in Anderson. Accordingly, claims 28-29 and 49 are not obvious over Anderson in view of Gamble and this rejection should be withdrawn.

Claims 28, 44 and 53 were rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al in view of Farr (US Patent No. 3,969,250, issued 13 July 1976). As explained above, Anderson et al fails to teach or suggest the production of an addressable array of oligonucleotides. As Farr was cited solely for the asserted teaching of a pressure gradient, Farr fails make up for the above

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deficiency in Anderson. As such, claims 28, 44 and 53 are not obvious over Anderson in view of Farr and this rejection may be withdrawn.

***Double Patenting***

The Examiner stated that the previous rejections under the judicially created doctrine of obviousness-type double patenting are maintained. The Examiner notes that Applicants stated on page 12 of the Remarks filed March 6, 2007 that a Terminal Disclaimer has been filed. However, no Terminal Disclaimer has been received by the Examiner, nor have any fees for the filing of a Terminal Disclaimer been paid.

Solely to expedite prosecution, the Applicants provide herewith a Terminal Disclaimer over U.S. Patent Application Nos. 11/234,701, 10/813,337, 10/813,331 and 10/449,838.

The Applicants note that the filing of a Terminal Disclaimer to obviate a rejection based on non-statutory double patenting is not an admission of the propriety of the rejection.<sup>1</sup> As such, while the Applicants firmly believe that this rejection fails to meet the requirements for Obviousness-Type Double Patenting set forth in MPEP § 804, a Terminal Disclaimer is nevertheless filed.

Accordingly, in view of terminal disclaimer(s) filed herewith, the Applicants respectfully request that this rejection be withdrawn.

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<sup>1</sup> *Quad Environmental Technologies Corp. v. Union Sanitary District*, 946 F.2d 870, 20 USPQ2d 1392 (Fed. Cir. 1991). The court indicated that the "filing of a terminal disclaimer simply serves the statutory function of removing the rejection of double patenting, and raises neither a presumption nor estoppel on the merits of the rejection."

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**CONCLUSION**

In view of the amendments and remarks above, the Applicants respectfully submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone Bret Field at (650) 327-3400.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-1078.

Respectfully submitted,

Date: July 9, 2007

By:

Bret E. Field  
Registration No. 37,620

Enclosures:

Enclosure(s): Terminal Disclaimer(s) as to U.S. Patent Application Nos. 11/234,701, 10/813,337, 10/813,331 and 10/449,838.

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